Does White Matter Hyperintensity Location predict Cognitive Impairment?

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INTRODUCTION

- **White matter hyperintensities (WMH)** are the most common **neuroimaging feature** of cerebral small vessel disease[1].
- They are associated with lacunar stroke, dementia and cognitive impairment[2,3].
- **Increasing volume** of WMH predicts **poorer cognition[1]**, but the association is **inconsistent[1,4]**.
- Development of **voxel-based analysis methods** has allowed study of the impact of WMH location.
- Previous research suggests the **location** of WMH may significantly affect cognition, especially frontal regions, but the **data is limited[4]**.

QUESTIONS

1. Does the **location** of WMH significantly predict cognitive impairment?
2. Is WMH presence in **specific white matter tracts** more important for cognitive impairment?

METHODS

WHO?
Sample from the ADNI database[5] of **599 elderly participants** split into:
- cognitively normal (n=191)
- cognitively impaired (n=408).

IMAGING
MRI FLAIR and T1 images were used to create **WMH lesion binary maps** *(lesion present or absent in a specific voxel)* (figure 1).

COGNITION
Montreal cognitive assessment (**MoCA)** scores used to identify cognitive impairment.

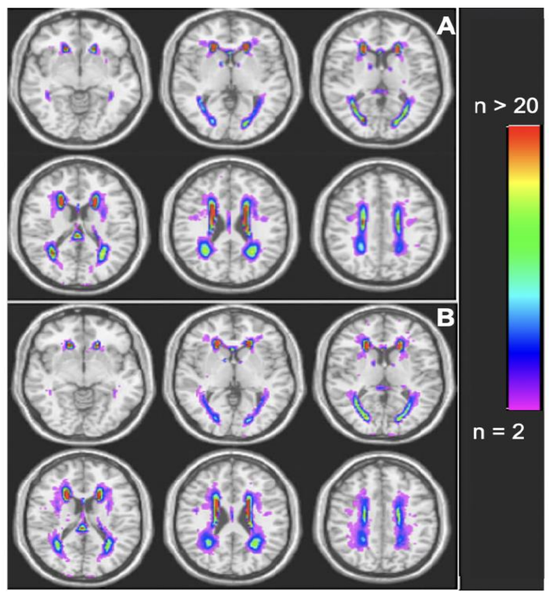
STATISTICAL ANALYSIS

VOXEL-BASED ANALYSIS
(all participants (n=599))
- Participant binary maps **multiplied by a MoCA z-score** (adjusted against the mean for cognitively normal group).
- **Mean weighted z-score** for each voxel of all participants produced an overall **cognitive risk map** (figure 2)**.**

TRACT-BASED ANALYSIS
(only cognitively impaired (n=408))
Multiple linear regression model:
- **Independent variable:** white matter tract percentage WMH occupancy (26 tracts).
- **Dependent variable:** MoCA score.
- **Covariates:** age, gender, education, amyloid status, APOE, grey matter volume and total WMH volume.

RESULTS

WMH binary lesion maps according to cognition



Both groups WMH percentage frequency look remarkably similar. Bilateral frontal regions are affected and those nearest the lateral ventricles.

Figure 1. WMH Frequency Maps. Colour bar= percentage frequency of participants with WMH in a voxel. (A) Cognitively impaired group (n=408) (B) Cognitively normal group (n=191).

Voxel-based analysis

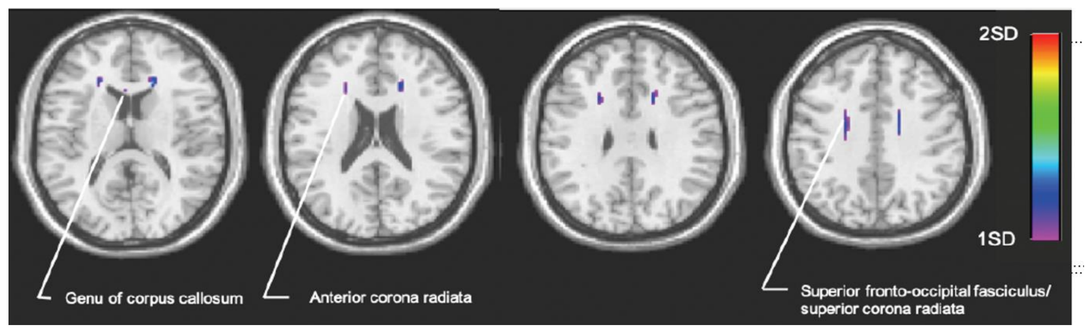


Figure 2. WMH cognitive risk maps of all participants (n=599). Voxels represent mean WMH-weighted MoCA-z score. Threshold set above 1 standard deviation (purple) up to 2 standard deviations from the mean (red). White matter tracts they project onto are labelled.

Clusters of voxels, located mainly in the anterior and superior corona radiata, were associated with worse cognition.

Tract-based analysis: multiple linear regression

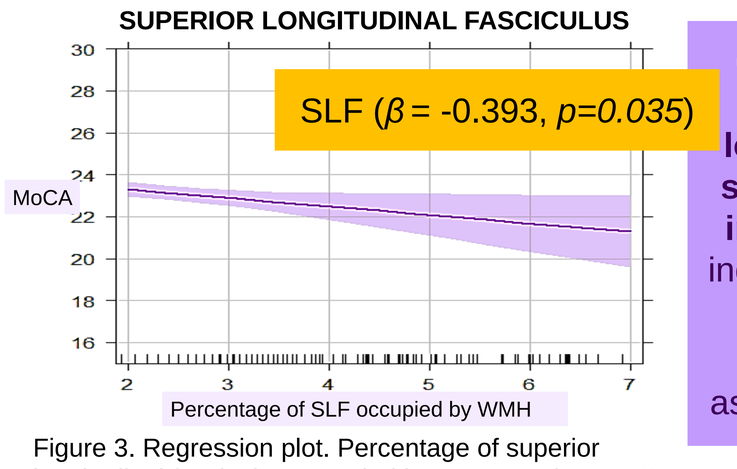


Figure 3. Regression plot. Percentage of superior longitudinal fasciculus occupied by WMH against MoCA.

Out of 26 tracts tested, **WMH in the superior longitudinal fasciculus significantly negatively impacted MoCA score,** independent of covariates.

No other tracts had a significant negative association with cognition.

CONCLUSIONS AND FUTURE DIRECTIONS

1**. Frontal WMH** appear particularly important in terms of impact on cognition.

2. The **superior longitudinal fasciculus** (SLF) may be a critical tract for cognitive impairment if affected by WMH, which agrees with previous work[6]. The SLF is proposed to be the main cortico-association fibre in the brain[7] and may therefore be important for **maintaining higher level cognitive function.**

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